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CBT for Nightmares in OEF/OIF Veterans

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14. ABSTRACT

This study examines the efficacy of two cognitive-behavioral treatments for PTSD-related recurrent nightmares and other sleep difficulties in veterans of Operations Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) in a randomized controlled trial. Participants will be 160 OEF/OIF veterans presently in outpatient treatment for PTSD at one of two study sites, the Philadelphia VAMC or the VACHS, West Haven, CT.

During Year One of this award, the study procedures have received approval by four regulatory bodies (PVAMC IRB, VACHS IRB, Yale University IRB and DoD HRPO). Further, the study was launched at the Philadelphia site and enrollment is under way. Data will be analyzed at the end of the data collection period and therefore research findings are not yet available.

15. SUBJECT TERMS
Posttraumatic Stress Disorder, Nightmares, Randomized Controlled Trial, Cognitive-behavioral Treatment, OEF/OIF Veterans

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Section I: Introduction

A substantial proportion of veterans returning from Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) have significant psychological symptoms related to traumatic war zone exposure, including recurrent nightmares and other sleep disturbances. Nightmares are generally distressing and difficult to treat, often persisting despite successful resolution of other Posttraumatic Stress Disorder (PTSD) symptoms. A cognitive-behavioral treatment (CBT), Imagery Rehearsal (IR), appears to have promise for successfully treating nightmares. This study investigates the efficacy of IR in treating OEF/OIF veterans, many of whom likely have mild to moderate traumatic brain injury (TBI). There are three main objectives of this study: 1) to examine the efficacy of IR, combined with psychoeducation about PTSD and nightmares and standard CBT for insomnia (IR + PPCI), compared to psychoeducation about PTSD and nightmares and CBT for insomnia (PPCI) alone, in reducing nightmare frequency and improving global sleep quality in OEF/OIF veterans with PTSD; 2) to determine whether there are moderating effects of neurocognitive impairment on the efficacy of these two forms of CBT for nightmares; and 3) to explore possible neurobiological correlates of treatment-related changes in nightmare frequency and sleep quality, focusing on noradrenergic systems. One hundred and sixty OEF/OIF veterans enrolled in treatment for PTSD at the Philadelphia VA Medical Center (PVAMC) or the VA Connecticut Health Care System (VACHS), West Haven Campus, will be randomized to one of two individual treatments: IR + PPCI or PPCI alone. Participants are referred by their mental health treatment providers and assessed for PTSD and war zone-related nightmares. Participants complete a battery of computerized neuropsychological tests at baseline and are stratified in their randomization to either group depending on the results. Once randomized, participants meet for 6 weekly individual sessions of IR + PPCI or PPCI alone. Participants complete self-report questionnaires assessing nightmares, sleep quality, PTSD, and depression, at baseline, immediately after treatment, and again three and six months after treatment. Additionally, participants provide saliva samples for measurement of salivary alpha-amylase, a marker of peripheral noradrenergic activity, both before sleep onset and upon awakening, for two nights before treatment and for two nights before the first post-treatment assessment.

Section II: Progress to Date on 5 Study Tasks in Approved Statement of Work:

1. Obtaining approvals for the study protocol at the study locations.

A. Philadelphia VAMC/University of Pennsylvania:

- Regulatory review of the initial protocol was completed by the PVAMC IRB on 3/13/2008 and the DoD HRPO on 2/13/2009. During the current reporting year, we have submitted the following amendments to this protocol: Amendment of research staff form/Addition of therapist (7/22/09), Request for obtaining Proxy Contact information (8/4/09), Room change (10/13/09), Request for pre-screening computerized records (11/16/09), Change in inclusion criteria (12/21/09), permission for electronic transfer of recordings (2/15/10), Amendment

of research staff form/Addition of new therapist (2/24/10), Clarification of TBI exclusion criterion (3/5/10), Addition of new recruitment sites at the PVAMC (5/17/10, pending approval).

B. VACHS, West Haven/Yale University:

- Regulatory review of the initial protocol was completed by the VACHS IRB and Research and Development Committee on 6/5/2008 and by the Yale University IRB on 11/12/2008. The DoD HRPO approved this protocol on 2/24/2009. The following amendments were submitted to this protocol: Addition of new staff members, Digital recording, Changes in procedures and testing battery (9/30/09); Request for pre-screening computerized records (1/21/10); Addition of proxy contact, Change in inclusion criteria, Change in method of participant payment (4/15/10); Electronic transfer of recordings, Change in supervisor (5/15/10).

- **PROBLEMS ENCOUNTERED:**
  Delay in start-up: Although a research coordinator was hired 7/1/09 and a therapist and an assessor joined the staff on 9/1/09, recruitment of participants did not commence until November 2009. The submission of necessary amendments to the study protocol precluded recruitment until that time. The three postdocs and Dr. Harpaz-Rotem came to Philadelphia for a two-day training team meeting on September 30 and October 1, 2009.

2. Recruitment, assessment and randomization of 80 participants at the PVAMC site and 80 at the VACHS site (total N=160).

A. Philadelphia VAMC:

- The PVAMC site has received 59 referrals from treatment providers during the reporting period. Eighty-six percent (51) were male, and 14% (8) were female. Forty-seven % (28) were African- American, 3% (2) Hispanic, 46% (27) Caucasian, 2% (1) Asian, and 2% (1) of other ethnic background.
- Assessments were scheduled with 26 potential participants: fifteen completed the first assessment, and nine veterans completed the second assessment as well. Eight participants were enrolled in the treatment study in the past year: four were randomized to IR + PPCI and four to PPCI alone.
- **PROBLEMS ENCOUNTERED:**
  - Technical issues: We concluded the lengthy process of obtaining approvals for digital videotaping and electronic transfer of recordings with the PVAMC IRB and the PVAMC IT and Information Security departments.
  - Recruitment challenges: As many other investigators (and VA clinicians) across the country have reported, we have faced difficulties recruiting and retaining participants from this younger group of veterans. This group of veterans is often ambivalent about treatment, and they have many other life responsibilities that may preclude consistent treatment seeking and treatment attendance. Early on in this contract year we recognized this as a major issue

for the recruitment for our study. After consultation with other researchers and clinicians, we have taken several steps to increase our recruitment rate. First, we increased our referral base by reaching out to different departments within the PVAMC, such as the Post-deployment clinic, the Polytrauma team, and the Multi-service Center in Philadelphia. We also have sought referrals from the local Vet Centers, and Dr. Ross has visited one Vet Center on two occasions to meet with the therapists. . Second, we amended our protocol to make our criteria more consistent with the realities of the study population. We now allow current alcohol and cannabis abuse. We clarified the criteria for diagnosing mild to moderate head injury. Third, we are now allowed to scan the computerized record to alert clinicians to upcoming appointments with potential candidates for referral to the study. Fourth, and we believe most important, we are currently expanding our recruitment sites to include the four PVAMC-affiliated community-based outreach clinics (CBOCs) around Philadelphia. We have reason to believe that OEF/OIF veterans are more likely to seek treatment outside of the city and closer to their homes, where parking is available, traffic is not too stressful and negotiating a major medical center is not required.

B. <u>VACHS, West Haven:</u>

- The VACHS site has received 22 referrals from treatment providers in the Mental Health Clinic. The site also received 14 self-referrals (i.e., veterans who contacted the study coordinator directly based on flyers advertising the study posted in the hospital). Of the referrals, 89% were male, and 11 % were female, with an average age of 35. Fifty-eight and three tenths percent were Caucasian, 22.2% African-American, and 19.4% Hispanic/Latino. Assessments were scheduled with 10 potential participants. All ten completed the first assessment, and six veterans completed the second assessment as well. Six participants were enrolled in the treatment study.
- Regular bi-site conference calls have served to help the VACHS site complete its set-up and to adapt procedures that the PVAMC site has found helpful for boosting recruitment. These calls have also served to obtain information regarding the comparability of all study procedures at the two sites. We have had 14 teleconferences, on the following dates: July 9, 2009; July 31, 2009; August 20, 2009; September 1, 2009; September 30, 2009; October 22, 2009; November 19, 2009; December 3, 2009; December 17, 2009; January 1, 2010; January 21, 2010; February 11, 2010; March 11, 2010; and March 25, 2010.
- The VACHS study team has reached out to primary care physicians to obtain referrals. Like the PVAMC site, it has amended its protocol to allow for the inclusion of alcohol and cannabis abuse in study participants. It has obtained permission to pre-screen the computer record so that clinicians can be advised of upcoming appointments with patients who may be appropriate referrals.

3. Administration of six sessions of the protocol treatments to participants.

A. <u>Philadelphia VAMC:</u>

- Of the eight enrolled veterans one is currently scheduled to begin treatment and seven have completed all six sessions of treatment. No veterans have withdrawn from the study this year.
- During year one of this award, a detailed supervision plan as well as fidelity rating procedures were developed, and implementation of these has begun.
- Weekly supervision calls with study supervisors, Drs. Philip Gehrman and Andrea Phelps, were attended by all therapists at both sites and have ensured treatment protocol adherence across sites.

B. VACHS, West Haven:

- Of the six participants enrolled in the treatment study four were randomized to IR + PPCI and two to PPCI alone. Five enrolled veterans are currently participating and have completed all six treatment sessions. One veteran withdrew after completing one session of treatment (IR + PPCI). We have unsuccessfully attempted to contact the veteran for follow-up assessments for ITT analyses.

4. Follow-up: re-assessment for detection of treatment effects and maintenance of benefits immediately post-treatment, and at 3 months and 6 months post-treatment.

A. Philadelphia VAMC:

- Of the eight enrolled veterans, seven veterans have completed treatment and are in the follow-up phase of the study. All seven have completed the first post-treatment session, three have completed the 3-month follow-up, and three have completed the 6-month follow-up.

B. VACHS, West Haven:

- Five participants have completed the first post-treatment assessment and are in the follow-up phase of the study. Three veterans have also completed the 3-month follow-up.

5. Statistical analysis of the data and manuscript preparation.

- The project is in the data collection phase, and no statistical analyses currently are being done.

Philadelphia VAMC:

- Entryof data from assessed and enrolled participants has commenced at the PVAMC now that the Access Database has been been completed and approved by study statisticians. Trouble-shooting of the database is ongoing with PVAMC IT staff.

Section III: Key Research Accomplishments:

- Completion of lengthy regulatory reviews at 3 institutions.
- Hiring and training of staff at both sites, including a bi-site training conference
- Participant recruitment at both sites has begun.

- Extensive efforts to boost recruitment rates; this has involved making necessary modifications to study protocols.
- Upcoming shift of recruitment from the VACHS site, which will not continue to recruit participants for the study, to PVAMC-affiliated CBOCs..

Section IV: Reportable Outcomes: Presentations:
None

Section V: Conclusions:
During this contract period, both sites recruited participants for the study. We enrolled 14 participants in total during the reporting year, with 12 participants completing active treatment and continuing in the follow-up phase of the study.

Early in the contract year, the PVAMC site began to identify barriers to recruitment and continuously devised plans to boost recruitment rates. These included amending the research protocol to allow for the inclusion of veterans who may currently abuse alcohol or cannabis and clarifying the criteria for including veterans with mild to moderate head trauma. Furthermore, we have reached out to providers in the Post-deployment and Polytrauma clinics and have obtained approval to pre-screen computerized records of veterans seen in the Mental Health Clinic in order to alert clinicians to potentially appropriate referrals to our study. Finally, we are currently expanding our recruitment to the four PVAMC-affiliated CBOCs around Philadelphia. Because more OEF/OIF veterans are seen for treatment in these clinics outside the city, we are hopeful that this change will increase our recruitment rates substantially.

In order to most efficiently conclude this project, we have decided to shift recruitment from the VACHS entirely to Philadelphia. We will expand recruitment in the Philadelphia area to the CBOCs at Ft. Dix, NJ, Horsham/Willow Grove, PA, Camden, NJ, and Gloucester, NJ (protocol amendment is awaiting approval by the PVAMC IRB). We have consulted with three psychologists who are stationed at these clinics and have determined that subject recruitment and enrollment and data collection at the clinics is feasible. We have been assured that our overall recruitment rate will increase substantially and that the rate of “no-shows” for appointments will be low. These three psychologists have agreed to serve as therapists for the study, and they will receive training within the next couple of months. . We are in the process of stream-lining procedures for the assessment and consenting of participants, and we will hire a full time employee dedicated to assessment and recruitment at these clinics. We envision beginning recruitment at the CBOCs in early Fall 2010.

Given the major expansion of recruitment to include several new sites in the Philadelphia area, just now getting underway, we anticipate that we will require additional time to meet our enrollment goal. We plan to apply for a no-cost extension of the project to enable us to enroll the projected number of participants and to conclude the project by June 30, 2013.